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Comparative Efficacy and Safety of Biologics and Small Molecule Inhibitors in the Treatment of Moderate-to-Severe Psoriasis: A Systematic Review

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Introduction
Psoriasis is a chronic, immune-mediated inflammatory skin condition affecting a significant portion of the global population. The condition results in substantial impairment of patients' quality of life and is associated with several comorbidities. The development of biologics and small molecule inhibitors has revolutionized the treatment landscape, offering targeted therapies with improved efficacy compared to traditional treatments. This systematic review evaluates the comparative efficacy and safety profiles of biologic therapies and small molecule inhibitors for the management of moderate-to-severe psoriasis.

Materials and Methods
A systematic review was performed across multiple databases, including PubMed, Web of Science, and Scopus, to identify randomized controlled trials (RCTs) comparing biologic agents and small molecule inhibitors in the treatment of moderate-to-severe psoriasis. The primary focus was on assessing treatment efficacy, as measured by the Psoriasis Area and Severity Index (PASI), and safety outcomes. Secondary endpoints included long-term treatment durability and patient-reported outcomes.

Results
The review included 22 head-to-head RCTs, involving over 50,000 patients. Among biologics, IL-17 inhibitors (Secukinumab, Ixekizumab) and IL-23 inhibitors (Guselkumab, Risankizumab) demonstrated superior efficacy in achieving PASI 90 and PASI 100 responses when compared to TNF-α inhibitors (Adalimumab, Etanercept). In particular, Secukinumab and Guselkumab exhibited higher rates of complete skin clearance (PASI 100) at Week 48. Among small molecule inhibitors, Deucravacitinib was found to be more effective than Apremilast in achieving PASI 75 and Static Physician Global Assessment (sPGA) responses. The safety profiles of these therapies were generally comparable, with mild injection-site reactions and nasopharyngitis being the most common adverse events. IL-17 inhibitors, however, were associated with a higher incidence of Candida infections.

Conclusions

IL-17 and IL-23 inhibitors show superior long-term efficacy compared to TNF-α inhibitors in treating moderate-to-severe psoriasis, with IL-23-targeting agents offering enhanced disease control. Small molecule inhibitors like Deucravacitinib present promising alternatives, especially for patients seeking effective oral therapies. Further research is required to compare TYK2, JAK, and PDE4 inhibitors with IL-17 and IL-23 agents in head-to-head trials, to refine clinical treatment strategies for psoriasis.